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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 12/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/051,952	WALKER, PATRICIA S.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *13-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1/17/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-14, botulinum toxin A as the clostridial toxin, and wrinkles and brow furrows as the condition to be treated in the response filed October 20, 2003 is acknowledged. The traversal is on the ground(s) that the claims of Groups II and III, which are directed to clostridial neurotoxin DNA, are closely related to the claims of Group I directed to clostridial neurotoxin protein, a search of one group of claims would encompass a search for the other two groups of claims; if patentability of botulinum toxin type A is indicated, claims directed to other toxin serotypes (B to G) should also be allowed because the botulinum toxins are a family of toxins having the same function; all the diseases or conditions cited are treated by a similar process of administering a clostridial neurotoxin protein or DNA to a subject via needleless injection. This is not found fully persuasive because the protein and DNA, which are functionally and structurally different chemical entities and have different utilities, are patentably distinct. Restriction is proper when two or more claimed inventions are either independent **or** distinct. See MPEP 803. Furthermore, coexamination of each of additional groups would have required a search of additional classes. For example, if Groups II and III were included, it would require additional searches for class 536/23.7 and 514/44. Regarding the diseases, each disease has different cause, may use different drug for treatment and has different outcome in the treatment; and if additional diseases were included, it would have required a search of these diseases. Therefore, coexamination of each of these inventions would require a serious additional burden of search. Regarding botulinum toxins, the argument is persuasive, thus botulinum toxins A-G are included for examination. Claims 15-35

of Groups II and III, and claims 13-14 of Group I are non-elected inventions, thus, withdrew from consideration. Claims 1-12, botulinum toxins A-G, and wrinkles and brow furrows are examined.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

2. Claim 1 is objected to because of the misspelled word "involontary".

3. Claims 5, 10 and 11 are objected to because the claim contains recitation of non-elected inventions.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating wrinkles and brow furrows in a human subject comprising administering botulinum toxin type A to a patient using a needleless syringe as indicated in the prior art, does not reasonably provide enablement for a method for treating a condition of an involuntary muscle contraction in an animal or human subject, wherein the method comprises administering a clostridial neurotoxin component to the subject using a needleless syringe, where the condition and the clostridial neurotoxin component are not defined. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-12 are directed to a method for treating a condition of an involuntary muscle contraction in an animal or human subject and the method comprises administering a clostridial neurotoxin component to the subject using a needleless syringe. The specification, however, only discloses cursory conclusions (page 12, line 33-page 13, line 36) without data supporting the findings, which state that the present invention provides a method for treating a condition of involuntary muscle contraction using a clostridial toxin component optionally coated on a carrier with a needleless syringe. There are no indicia that the present application enables the full scope in view of the method for treating a condition of involuntary muscle contraction by administering a clostridial toxin component with a needleless syringe as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the presence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding the conditions of involuntary muscle contraction being treated, and the clostridial toxin components or variants thereof being administered, which are not adequately described or demonstrated in the specification.

(2). The presence or absence of working examples:

The specification demonstrates the use of botulinum toxin type A in the treatment of pain associated with muscle disorders, and hyperhidrosis (Examples 1-10). There are no other working examples indicating the variants in association with the claimed methods.

(3). The state of the prior art and relative skill of those in the art:

The prior art (e.g., Borodic, U. S. Patent 5,183,462; Vadoud-Seyedi *et al.*, Dermatology 201, 179, September 2000; McCabe *et al.*; U. S. Patent 5,525,510) teaches the use of botulinum toxin type A with a needleless syringe in the treatment of wrinkles and brow furrows. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the treating conditions for various clostridial toxin components and variants thereof, and the effects of the clostridial toxins in the treatment of various conditions of involuntary muscle contraction to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass the use of various clostridial toxin components, but the treating conditions such as the dose and the time, and the effects of the toxins are not described in the specification, thus the invention is highly unpredictable regarding the outcome of the treatment.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method for treating a condition of an involuntary muscle contraction in an animal or human subject and the method comprises administering a clostridial neurotoxin component to the subject using a needleless syringe. The specification indicates the clostridial toxin components used in the treatment may comprise a targeting component, a

therapeutic component and a translocation component, which may be a segment of light chain or heavy chain of various clostridial toxins or a variant thereof (pages 14-17), and Examples 1-10 have shown the use of botulinum toxin types A in the treatment of pain associated with muscle disorders and hyperhidrosis with a needleless syringe. However, the specification has not demonstrated the treatment of various conditions associated with an involuntary muscle contraction using various clostridial toxin components or variants thereof with a needleless syringe, nor has indicated the treating conditions such as the dose, the time and effects of these toxins. Moreover, there are no working examples indicating the claimed methods associated with the variants. Since the specification has not provided sufficient teachings on the treating conditions for various clostridial toxin components other than botulinum toxin type A, and the effects of these components. Therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the in effects of various clostridial toxin components and variants thereof in the treatment of conditions associated with an involuntary muscle contraction.

(6). Nature of the Invention

The scope of the claims includes the use of many clostridial toxin variants, however the specification has not demonstrated the use and the effects of these variants. Thus, the disclosure is not enabling for reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed methods, the outcome of the treatment is unpredictable and the teachings in the specification are limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effects of various clostridial toxin components in the claimed method.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claims 1-12 are indefinite because the claims lack essential steps in the method of treating a condition related to involuntary muscle contraction in a subject. The omitted steps are: an effective amount of a clostridial neurotoxin component used, and the outcome of the treatment. Claim 1 is also indefinite because of the use of "a Clostridial neurotoxin component", it is not clear whether the Clostridial neurotoxin component contains the whole toxin, the targeting component, the therapeutic component, or the translocation component. Claims 2-12 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

7. Claim 4 is indefinite because of the use of the term "preferably solid and/or metallic material". The term "preferably solid and/or metallic material" renders the claim indefinite, it is unclear what other materials of the carrier are used for comparison as to "preferably solid and/or metallic material", and whether the limitation after "and/or" is included or not, and if included is to be read as an alternative "or" or the conjunctive "and".

8. Claim 8 is indefinite because of the use of the term "administered to a skin and substantially to a muscle tissue". The term "administered to a skin and substantially to a muscle

tissue" renders the claim indefinite, it is unclear to what extent the neurotoxin component is administered to the muscle tissue as to "substantially".

9. Claim 10 is indefinite because of the use of the term "a variant thereof". The term " a variant thereof" renders the claim indefinite, it is unclear how different the variant is from the parent compound, and what amino acid sequence the variant has since neither the specification nor the claim indicates how many amino acids and what amino acids are modified in the neurotoxin component (page 21, lines 1-14 of the specification).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1, 2 and 5-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Borodic (U. S. Patent 5,183,462) taken with Vadoud-Seyedi *et al.* (Dermatology 201, 179 (September 2000)).

Borodic discloses the injection of an appropriate dose of a botulinum toxin such as pharmaceutical grade botulinum toxin type A to interrupt nerve impulse transmission across the neuromuscular junction (column 4, lines 50-58; claim 7) and to attenuate tone of muscles about the eyes and forehead can remove wrinkles and brow furrows (column 3, line 67-column 4, line 6; column 9, lines 42-66; claims 1, 5, 8-12). However, Borodic does not disclose the use of a needleless syringe. Vadoud-Seyedi *et al.* disclose mouse botulinum toxin A in NaCl solution is injected into patients with plantar hyperhidrosis with a Dermojet (a needleless injection system;

the whole document; claims 2 and 6). At the time of invention was made, it would have been obvious to one of ordinary skill in the art to treat wrinkles and brow furrows by administering botulinum toxin A as taught by Borodic with a Dermojet as taught by Vadoud-Seyedi *et al.* because the injection of botulinum toxin with a Dermojet is an effective and comfortable technique for administration of botulinum toxin for cosmetic purposes. Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

11. Claims 3 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Borodic in view Vadoud-Seyedi *et al.* as applied to claims 1, 2 and 5-12 above, further in view of McCabe *et al.* (U. S. Patent 5,525,510).

Borodic discloses the injection of an appropriate dose of a botulinum toxin such as pharmaceutical grade botulinum toxin type A to interrupt nerve impulse transmission across the neuromuscular junction (column 4, lines 50-58; claim 7) and to attenuate tone of muscles about the eyes and forehead can remove wrinkles and brow furrows (column 3, line 67-column 4, line 6; column 9, lines 42-66; claims 1, 5, 8-12); and Vadoud-Seyedi *et al.* disclose mouse botulinum toxin A in NaCl solution is injected into patients with plantar hyperhidrosis with a Dermojet (claims 2 and 6). However, Borodic and Vadoud-Seyedi *et al.* do not disclose the use of a botulinum toxin coated onto the carrier. McCabe *et al.* teach the biological material such as DNA, RNA, proteins or peptides is coated onto the carrier particles such as small gold beads or spheres (column 6, lines 22-35; claims 3 and 4). At the time of invention was made, it would have been obvious to one of ordinary skill in the art to treat wrinkles and brow furrows using the method taught by Borodic and Vadoud-Seyedi *et al.* with botulinum toxin A coated onto the gold

sphere taught by McCabe *et al.* because the treatment with neurotoxin coated onto the gold particle would be safer since the high density carrier with small particle size would readily enter living cells without injuring the cells. Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

Conclusion

12. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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December 7, 2003